Kocaeli Med J 2019; 8; 2:126-133

Yaşlanma ile İlişkili Basit ve Yeni bir Parametre: Desendan Aorta Sürekli Dalga Doppler Sistolik Pik Gradient

Simple and New Echocardiographic Parameter Related to Aging: Descending Aortic Continuous Wave Doppler Systolic Peak Gradient

Onur Argan[1], Serdar Bozyel[2]

[1]Balıkesir Üniversitesi Tıp Fakültesi, Kardiyoloji Ana Bilim Dalı, Balıkesir, Türkiye
[2]Derince Eğitim Araştırma Hastanesi, Kardiyoloji Ana Bilim Dalı, Kocaeli, Türkiye

ÖZ

GİRİŞ ve AMAÇ: *Artan insan ömrü nedeniyle dünyadaki yaşlı popülasyon hızla artmaktadır. Yaşlanma ile ilgili yeni parametreler yaşlanmanın fizyopatolojisini ve kardiyovasküler hastalıklardan korunmada fayda sağlayabilir. Bu çalışmanın amacı yaşlanma ve yaşlanma ile ilişkili hastalıklar ile desendan aorta CW doppler sistolik pik gradient arasındaki ilişkiyi saptamaktır.*

YÖNTEM ve GEREÇLER: *Çalışmaya 372 katılımcı dahil edildi. Aort koarktasyonu olan hastalar ve 18 yaş altı katılımcılar çalışma dışı bırakıldı. Yatar pozisyonda, suprasternal pencereden desendan aortaya paralel olarak sürekli dalga doppler ölçümleri kaydedildi. Aortik sürekli dalga doppler sistolik pik gradienti tüm katılımcılardan elde edildi. Katılımcıların karakteristikleri, ekokardiyografik, biyokimyasal parametreleri ile yaş arasındaki ilişki değerlendirildi.*

BULGULAR: *Desendan aortik sürekli dalga doppler sistolik pik gradyanı incelendiğinde yaş ile negatif (r =-0.499,p<0.001);kreatinin (r=-0.217,p <0.001); üre (r =-0.289,p<0.001); Hba1c (r = -0.252 p <0.001); LVEDD (r =-0.188, p<0.001); LVESD (r =-0.200,p <0.001); IVS (r=-0.259,p<0.001); PW (r =-0.248, p<0.001); LA (r=-0.272, p<0.001); PAP (r=-0.217, p<0.001); E / E '(r =-0.185, p<0.001), eGFR (Cockcroft-Gault mL / dk) (r =0.395,p <0.001) ve EF (r =0.266 p<0.001) ile pozitif korelasyon saptandı.*

MannWhitney U analizinde desendan aorta sürekli dalga doppler sistolik pik gradyanı hipertansiyon (p<0.001), koroner arter hastalığı (p <0.001), atrial fibrilasyon (p<0.001), ve sistolik kalp yetmezliği hastalarında (p<0.001) anlamlı olarak daha düşük saptandı. Stepwise lineer regresyon analizinde, desendan aorta sürekli dalga doppler sistolik pik gradientin ile yaş arasında bağımsız korelasyon saptandı (p<0.001).

TARTIŞMA ve SONUÇ: *Desendan aorta sürekli dalga doppler sistolik pik gradientinin ölçümü yaşlanma ile ilişkili noninvaziv, pratik, tekrarlanabilir ve basit bir yöntemdir. Bu parametre klinik pratikte yaşlanmanın bir göstergesi olarak kolayca kullanılabilir.*

Anahtar Kelimeler: *Yaşlanma, yaşlılık, Desendan aorta, sürekli dalga doppler*

ABSTRACT

BACKGROUND: *The world inhabitants increasing to grow older fastly, due to rising longevity. A new parameters related to cardiovascular aging may help to understand cardiac pathophysiology and prevention of cardiac disorders. The aim of the study was to find out a possible relationship between descending aortic continuous wave doppler systolic peak gradient and aging, age related illnesses.*

MATERIALS and METHODS: *The study group was composed of 372 people. Aortic coarctation patients and under 18 years old participants exluded to the study. Continuous wave doppler measurements from suprasternal window at supine position were recorded with the cursor parallel to main flow of direction in descending aorta. Descending aortic continuous wave doppler systolic peak gradient was obtained from all participants, and correlations were evaluated between participants caracteristics, echocardiographic, biochemical parameters and age.*

RESULTS: *When descending aortic continuous wave doppler systolic peak gradient was analyzed, there was negative correlations with age (r= -0.499, p<0.001); creatinine (r= -0.217, p<0.001); urea (r= -0.289, p<0.001); Hba1c (r= -0.252 p<0.001); LVEDD (r= -0.188, p<0.001); LVESD (r= -0.200, p<0.001); IVS (r= -0.259, p<0.001); PW (r= -0.248, p<0.001); LA (r= -0.272, p<0.001); PAP (r= -0.217, p<0.001); E/E' (r= -0.185, p<0.001), ascending aortic diameter (r= -0.269, p<0.001) and positive correlations with eGFR (Cockcroft-Gault mL/dk) (r= 0.395, p<0.001), EF (r= 0.266 p<0.001). In MannWhitney U test, descending aortic continuous wave doppler systolic peak gradient was significantly lower in HT (p<0.001); CAD (p<0.001); AF (p<0.001); systolic heart failure patients (p<0.001) when compared to those without this disease.In stepwise linear regression analysis, significant independent correlates of descending aortic continuous wave doppler systolic peak gradient was only age (p<0.001).*

CONCLUSION: *Measurement of descending aortic continuous wave doppler systolic peak gradient is noninvasive, practical, repeatable and simple method and independently related to the aging. Decreasing descending aortic continuous wave doppler systolic peak gradient measurements can be easily feasible in clinical practice as an indicator of aging.*

Keywords:, *Aging, elderly, descending aorta, continuous wave doppler.*

İletişim / Correspondence:

Dr. Onur Argan
Balıkesir Üniversitesi Tıp Fakültesi, Kardiyoloji Ana Bilim Dalı, Balıkesir, Türkiye
E-mail: onur_argan@yahoo.com
Başvuru Tarihi: 18.12.2017
Kabul Tarihi: 14.08.2019

INTRODUCTION

The world inhabitants not stopping to grow older fastly, due to rising longevity. There is an obvious relationship between aging and increasing cardiac disorders. Therefore ageing is the largest risk factor for cardiac diseases, the frequency of these diseases grows significantly with increasing age . For this reason, a new parameters related to cardiovascular aging may help to understand cardiac pathophysiology and prevention of cardiac disorders. So as to develop old patient care and forestall the age related cardiovascular disorders, new insight should bring valuable information leading to cardiovascular aging.

We categorized changes related to aging in the heart on functional, structural, cellular and hormonal. These factors may help to give reasons of the age related risk factors in cardiac diseases.

Echocardiography gives us an easy and noninvasive procedure for evaluating relation between aging and cardiac disorders.

In this study; we present the new and basic echocardiographic parameter related to aging: Descending aortic continuous wave (CW) doppler systolic peak gradient.

MATERIALS and METHODS

The study group was composed of 506 people who apply cardiology policlinics for any reason. Aortic coarctation patients and under 18 years old participants exluded to the study. 134 participants were excluded due to unclear suprasternal window appearance. All the 372 participants included in our study had echocardiographic images were of sufficient quality. Coronary artery disease (CAD) was defined as vessel with a stenosis ≥50% by quantitative coronary angiography or history of coronary artery bypass surgery and stenting. Transthoracic echocardiographic examination

All patients underwent conventional transthoracic echocardiography using Vivid-S5, GE Vingmed ultrasound with a broadband probe. Chamber diameters and ventricular function were assessed according to current guidelines.

Continuous wave doppler measurements from suprasternal window at supine position were recorded with the cursor parallel to main flow of direction in descending aorta. Routine biochemistry analysis were evaluated and estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft Gault formula.

Statistical analysis

All analyses were used the SPSS for Windows, version IBM 22.0. All variables were performed for normality using the Shapiro Wilk test. Continuous variables were demonstrated as median and 25th–75th percentiles; and categorical variables were given as percentages. For the comparison of patients with hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD) and atrial fibrillation (AF) were evaluated by Mann Whitney U test.

Statistically significance was defined if $p<0.05$ was found. Correlates of aortic valve continuous wave doppler systolic gradient were assessed with Spearman rank correlation test. Echocardiographic, biochemical, clinical variables with relationship to aortic valve continuous wave doppler systolic gradient was tested with stepwise linear regression analysis adjusted for age, eGFR, HbA1c, AF, HT, CAD, EF, hemoglobin, E/E'.

RESULTS

A total of 372 patients who met inclusion and exclusion criteria were included in the study. The baseline characteristics and medications, biochemical and echocardiographic parameters of the patients are summarized in Table 1-2-3 respectively.

When descending aorta continuous wave doppler systolic peak gradient was analyzed with the biochemical parameters, there was negative correlations with age ($r= -0.499$, $p<0.001$); creatinine ($r= -0.217$, $p<0.001$); urea ($r= -0.289$, $p<0.001$); Hba1c ($r= -0.252$ $p<0.001$); and positive correlations with eGFR (Cockcroft-Gault mL/dk) ($r= 0.395$, $p<0.001$). (Table 4) (Figure 1-2-3)

Table 1. Demographic data of the study group	
Age (years)	59 (46-71)
Gender (M/F)	228/278 (45.1%/54.9%)
Body Mass Index (kg/m2)	28.72 (25.39-32.63)
Coronary artery disease	90(18.1%)
Hypertension	260 (52.2%)
Diabetes Mellitus	131 (26.3%)
Obese (BMI of ≥30 kg/m2)	206 (40.8%)
Atrial fibrillation	116 (23.3%)
Acetylsalicylic Acid	87 (17.5%)
Warfarin	52 (10.4%)
Clopidogrel	27 (5.4%)
ACE-I/ARB	147(29.5%)
Spironolactone	25 (5%)
Calcium channel blocker(Dihidropiridin)	120 (24.1%)
B blocker	151 (30.3%)
Statin	83 (16.7%)
Nitrates	15 (3%)
Digoxin	9 (1.8%)
Thiazide	92 (18.5%)
Loop diuretic	58 (11.6%)
New oral anticoagulant	59 (11.8%)
Amiodarone	10 (2%)
Diltiazem	19 (3.8%)
İnsülin	32 (6.4%)
Oral antidiabetic	48 (9.6%)

Table 2. Biochemical data of the study group	
Glucose (mg/dL)	104.5 (95-119.75)
HbA1c	5.6 (5.3-6.2)
Sodyum (mEq/L)	140 (139-142)
Creatinine (mg/dl)	0.88 (0.75-1.05)
Urea (mg/dl)	33 (25-42)
eGFR (Co-Croft mL/dk)	93.52 (68.3-120.12)
Total Cholesterol (mg/dl)	194 (163.6-226.6)
LDL (mg/dl)	119.5 (93-148)
HDL (mg/dl)	44 (39-53)
Trigliserid (mg/dl)	129 (89-191.5)
WBC (uL)	6.9 (5.7-8.48)
AST (U/L)	21 (18-25)
ALT (U/L)	17 (13-23)
Platelet (uL)	248 (208.26-298)
TSH (IU/ml)	1.39 (0.95-2.19)
T3 (IU/ml)	2.8 (3.33-3.43)
T4 (IU/ml)	0.92 (0.81-1.03)
Hb (g/dl)	13.1 (12-14.3)
Hematocrit (%)	40.7 (37.1-43.95)

Table 3. Echocardiographical data of the study group	
LVEDD (mm)	46 (43-49)
LVESD (mm)	32 (28-36)
Ejection Fraction (%)	60 (55-65)
LA(mm)	35 (31-39)
RV(mm)	22 (20-24)
PAP (mmHg)	25 (20-30)
E/E'	9 (7.27-12)
IVS (mm)	10 (9-12)
PW (mm)	10 (10-12)
Tissue Doppler E' velocity (cm/s)	8 (7-10)
Descending aortic peak gradient (mmHg)	4,3 (3.2-6)

Table 4. Biochemical parameters correlated CW doppler descendan aortic peak gradient		
Age	Spearman Correlation	-0.499
	Sig. (2-tailed)	**<0.001**
eGFR (Cockcroft-Gault mL/dk)	Spearman Correlation	0,395
	Sig. (2-tailed)	**<0.001**
Urea (mg/dl)	Spearman Correlation	-0.289
	Sig. (2-tailed)	**<0.001**
Creatinine (mg/dl)	Spearman Correlation	**-0,217**
	Sig. (2-tailed)	**<0.001**
Hba1c	Spearman Correlation	-0.252
	Sig. (2-tailed)	**<0.001**

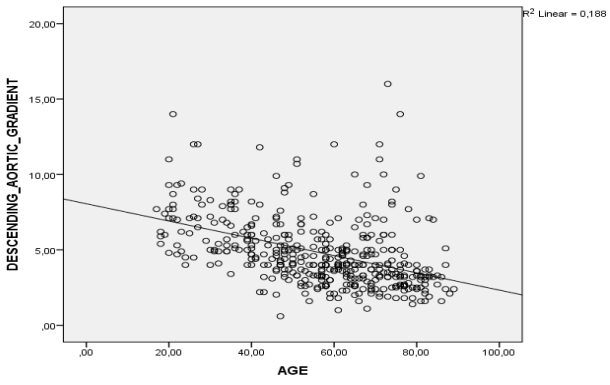

Figure 1. Relationship between descendan aortic CW doppler peak gradient and age

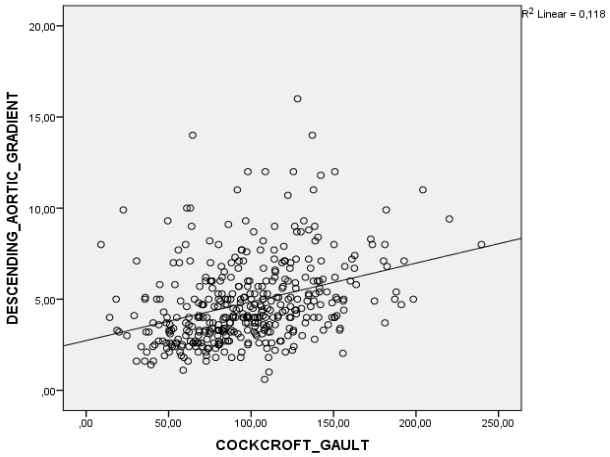

Figure 2. Relationship between descendan aortic CW doppler peak gradient and eGFR (Cockcroft Gault Formula)

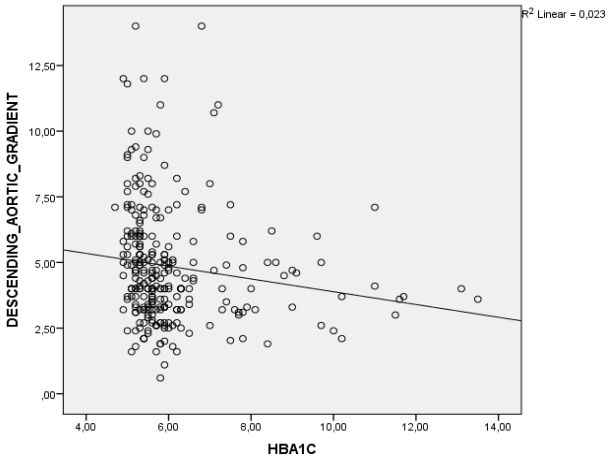

Figure 3. Relationship between descendan aortic CW doppler peak gradient and HbA1c

When descending aortic continuous wave doppler systolic peak gradient was analyzed with echocardiography parameters, there was negative correlations with left ventricle end diastolic diameter (LVEDD) (r= -0.188, p<0.001); left ventricle end systolic diameter (LVESD) (r= -0.200, p<0.001); interventricular septum diameter (IVSd) (r= -0.259, p<0.001); posterior wall diameter (PWd) (r= -0.248, p<0.001); left atrium diameter (LAd) (r= -0.272, p<0.001); pulmonary artery pressure (PAP) (r= -0.217, p<0.001); E/E' (r= -0.185, p<0.001); ascending aortic diameter (r= -0.269, p<0.001) and positive correlations with ejection fraction (EF) (r= 0.266, p<0.001). (Table 5) (Figure 4-5-6)

Table 5. Echocardiographic parameters correlated with descendan aortic CW doppler peak gradient

EF	Spearman Correlation	0,266
	Sig. (2-tailed)	**<0.001**
LVEDD	Spearman Correlation	-0,188
	Sig. (2-tailed)	**<0.001**
LVESD	Spearman Correlation	-0,200
	Sig. (2-tailed)	**<0.001**
IVS	Spearman Correlation	-0,259
	Sig. (2-tailed)	**<0.001**
PW	Spearman Correlation	0,248
	Sig. (2-tailed)	**<0.001**
LA	Spearman Correlation	-0,272
	Sig. (2-tailed)	**<0.001**
PAB	Spearman Correlation	-0,217
	Sig. (2-tailed)	**<0.001**
E/E'	Spearman Correlation	-0,185
	Sig. (2-tailed)	**<0.001**
E' wave	Spearman Correlation	0,402
	Sig. (2-tailed)	**<0.001**

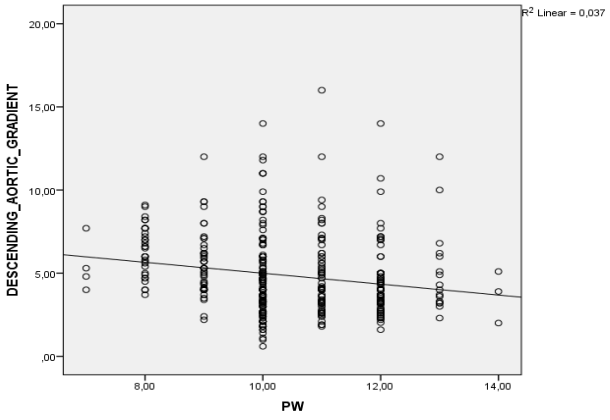

Figure 4. Relationship between descendan aortic CW doppler peak gradient and posterior wall diameter (PW)

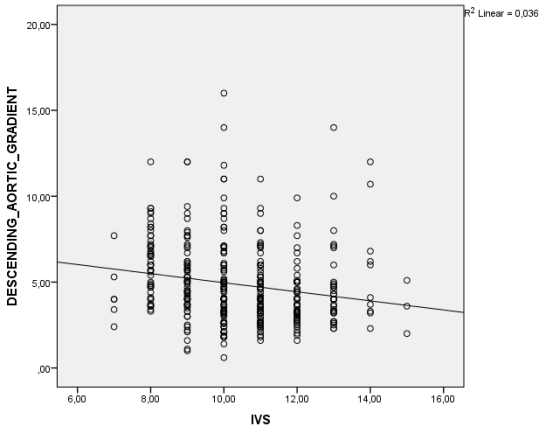

Figure 5. Relationship between descendan aortic CW doppler peak gradient and intervetricular septum diameter (IVS)

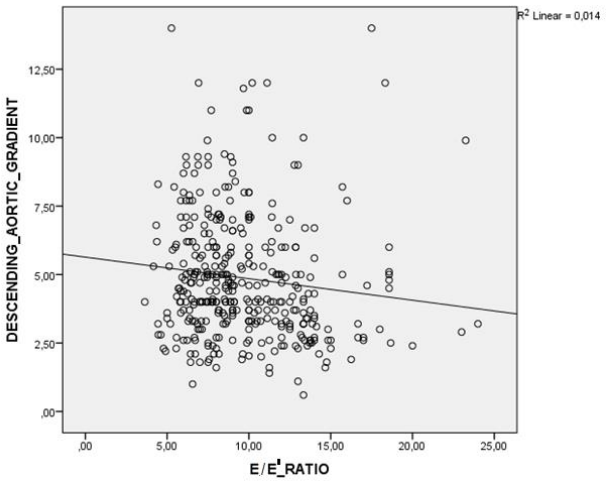

Figure 6. Relationship between descendan aortic CW doppler peak gradient and E/E' ratio

Descending aortic continuous wave doppler systolic peak gradient was significantly lower in hypertensive patients when compared to the nonhypertensive patients (MannWhitney U test; p<0.001); lower in patient with coronary artery disease when compared to the patient without coronary artery disease (MannWhitney U test; p<0.001); lower in patients with AF ryhthm when compared to the patients with sinus rhythm (MannWhitney U test; p<0.001); lower in heart failure patients (EF≤45%) when compared to the patients without heart failure (MannWhitney U test; p=0,010). There was not any relationship between gender (MannWhitney U test; p=0,190).

Echocardiographic, biochemical, clinical variables with relationship to aortic valve continuous wave doppler systolic gradient was tested with stepwise linear regression analysis adjusted for age, eGFR, HbA1c, AF, HT, CAD, EF, hemoglobin and E/E'. In stepwise linear regression analysis, significant independent correlates of descending aortic continuous wave doppler systolic peak gradient was only age (p<0.001).

DISCUSSION

We categorized changes related to aging in the heart on functional, structural, cellular and hormonal. On a structural level, the left ventricle wall thickens with aging as an outcome of increased cardiomyocyte magnitude.

Left atrial size stays nearly the same during all of the life in healty people ; and may not enlarge as an effect of advancing age, in spite of the diastolic dysfunction. In an advanced stages of life, atrial contraction plays an important role in diastolic phase in an old people.

Large left atrial diameter has been correlated with the development of the atrial fibrillation, indicating that atrial remodeling causes of the progression of an atrial fibrillation .

On a functional changes of the aging heart; left ventricle diastolic function decreases with aging 3-like the E' wave, proving reduced left ventricle relaxation. Hypertension, diabetes mellitus, obesity can increase these findings and may be designated to as risk factors for cardiac aging. Besides, E/E' rises with aging along with other parameters. During all of life, the left ventricle ejection fraction is maintained within normal limits. On the other hand, maximal exercise capacity reduces step by step, because of the reduction in contractile reserve 3-5- .

Cardiac aging causes morphological changes in the valves and 10 % of patients aged more than 50 years have mitral annular calcification .

Cardiac disorders are the primary reason of death in the old population. Patients with cardiovascular disorders over 60 years old, 70 % have atrial fibrillation, 75 % heart failure and 80 % ischemic heart disease . Aging is a major risk factor for all of them. Hypertension, diabetes mellitus, obesity,

hyperlipidemia and anemia stimulate the cardiac aging . Also, The incidence and prevalence of aortic aneurysms is low in the population under 60 years of age - . The incidence of aortic aneurysms increases with age.

In our study population, interventrivular septum and posterior wall were thicker, left atrial size was larger, E' wave was lower, E/E' was higher and ascending aortic diameter was larger in elderly participants than the young participants. There were more diabetes, hypertension, coronary artery disease, chronic kidney disease and atrial fibrillation in elderly participants than the young participants similar to the above findings.

On a hormonal, cellular and molecular chancing; oxidative stress, systemic inflammatory and endocrine disorders contribute to cardiac aging significantly - . Renin-angiotensin-aldosterone system and β-adrenergic system plays an critical role in regulating blood volume and systemic resistance.

Oxidative stress is related to the cardiac aging. Superoxide and hydrogen peroxide play the important role of age related damage and mitochondrial DNA damage. In addition hypertension, diabetes mellitus, obesity, dyslipidemia can speed up the cardiac aging.

Hearts and arteries are inseparable parts of a whole. The arteries has two main functions. First, arteries behave like pipes to carry blood to the distal tissues. Second, arteries act as a windkessel (hydraulic filter) to cushion blood flow and pressure oscillations for guaranting peripheral tissue perfusion at continuously circulation and pressure .

Due to the peripheric resistance, only some part of the stroke volume is towarded front straight to the peripheric tissues. 50% of stroke volume is stored in the aorta expanding the arterial walls and maintaining the blood pressure in diastolic period. 10% of the energy manifactured by the heart is stored in the arterial wall for this function. In diastolic period, by the stored energy, the accumulated blood into the aorta sends to the peripheric tissues and maintains the blood pressure. The effectiveness of this function is associated with the elastic ability of the vessel walls.

Articles related to arterial stiffness emphasize that the main factor affecting stiffness is ageing . The arterial walls become thicker and stiffer with ageing. Due to the degeneration of the elastic fibres in intima and media, vessel loses the elastic ability with aging.

Arterial stiffening is observed in a few diseases, including atherosclerosis, chronic kidney disease, hypertension and diabetes mellitus.

Cardiovascular aging can be evaluated by practice of arterial stiffness examination. Invasive and non invasive methods have been used for that evaluation. Widely used and comfirmed techniques contain pulse wave velocity assessment - - . However, when these studies are compared with our study, the method and application region used is different.

These outcomes propose that prevention of cardiac aging can decrease the possibility of future cardiac disorders. A protective diagnosis and treatment strategy to decrease cardiac aging may be consequential in the prevention of cardiac diseases especially in aging societies.

To solve this subject, studies that include effective prophylactic new parameters for aging will be needed.

It is a fact that HT, DM, chronic kidney disease, atrial fibrillation and heart failure are increasing with the age. Descending aortic continuous wave doppler systolic peak gradient was found to be lower in patients with these diseases in our study population. Besides, measurement of descending aortic continuous wave doppler systolic peak gradient is independently related to the aging.

Decreasing descending aortic continuous wave doppler systolic peak gradient measurements can be easily feasible in clinical practice as an indicator of aging and it can be used for risk scoring. Further studies are needed to assess importance of this parameter.

CONCLUSION

A new parameters related to cardiovascular aging may help to understand pathophysiology and prevention of cardiovascular diseases increasing with aging. Measurement of descending aortic continuous wave doppler systolic peak gradient is noninvasive, practical, repeatable and simple method and related to the aging and age-related illnesses directly. Descending aortic continuous wave doppler systolic peak gradient measurements can be easily feasible in clinical practice as an indicator of aging.

Conflict of interest:

There is no conflict of interest.

REFERENCES

1. Lakatta EG, Levy D (2003) Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: part II: the aging heart in health: links to heart disease. Circulation 107:346–354

2. Olivetti G, MelissariM, Capasso JM, Anversa P (1991) Cardiomyopathy of the aging human heart. Myocyte loss and reactive cellular hypertrophy. Circ Res 68:1560–1568

3. Daimon M, Watanabe H, Abe Y, et al. Normal values of echocardiographic parameters in relation to age in a healthy Japanese population: the JAMP study. Circ J. 2008;72:1859–66.

4. Lam CS, RienstraM, TayWT, Liu LC, Hummel YM, van der Meer P, de Boer RA, van Gelder I, Van Veldhuisen DJ, Voors AA, Hoendermis ES (2017) Atrial fibrillation in heart failure with preserved ejection fraction: association with exercise capacity, left ventricular filling pressures, natriuretic peptides, and left atrial volume. JACC Heart Fail 5:92–98

5. Daimon M, Watanabe H, Abe Y, et al. Gender differences in agerelated changes in left and right ventricular geometries and functions. Echocardiography of a healthy subject group. Circ J. 2011;75:2840–6.

6. Fleg JL, O'Connor F, Gerstenblith G, et al.

Impact of age on the cardiovascular response to dynamic upright exercise in healthy men and women. J Appl Physiol (1985). 1995;78:890–900.

7. Yutani C. Atlas of cardiac pathology. 1st ed. Bunkoudou: Department of Pathology, State Cardiovascular System Disease Center Japan; 1991. p. 257–259.

8. Dai DF, Chen T, Johnson SC, et al.

Cardiac aging: from molecular mechanisms to significance in human health and disease. Antioxid Redox Signal. 2012;16:1492–526.

9. Paulus WJ, Tscho¨pe C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular

endothelial inflammation. J Am Coll Cardiol. 2013;62:263–71.

10. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, et al; Multicentre Aneurysm Screening Study Group. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet 2002;360:1531–9.

11. Howard DP, Banerjee A, Fairhead JF, Handa A, Silver LE, Rothwell PM; Oxford Vascular Study. Population-Based Study of Incidence of Acute Abdominal Aortic Aneurysms With Projected Impact of Screening Strategy. J Am Heart Assoc 2015;4:e001926.

12. Loffredo FS, Nikolova AP, Pancoast JR, et al. Heart failure with preserved ejection fraction: molecular pathways of the aging myocardium. Circ Res. 2014;115:97–107.

13. Wu J, Xia S, Kalionis B, et al. The role of oxidative stress and inflammation in cardiovascular aging. Biomed Res Int. 2014;2014:615312.

14. Verbrugge FH, Tang WH, Mullens W (2015) Renin-Angiotensinaldosterone system activation during decongestion in acute heart failure: friend or foe? JACC Heart Fail 3:108–111

15. O'Rourke MF. Principles and definitions of arterial stiffness, wave reflections and pulse pressure amplification. In: Safar ME, O'Rourke MF (eds). Handbook of Hypertension (series editors: Birkenhäger WH, Reid JL), Vol. 23, Arterial Stiffness in Hypertension. Elsevier,

2006; 3–20

16. Guerin A, Blacher J, Pannier B et al. Impact of aortic stiffness attenuation on survival of patients in end-stage renal disease. Circulation 2001; 103: 987–992

17. London GM, Pannier B. Arterial functions: how to interpret the complex physiology. Nephrol Dial Transplant. 2010 Dec;25(12):3815-23. doi: 10.1093/ndt/gfq614.

18. Van Sloten TT, Schram MT, van den Hurk K, Dekker JM, Nijpels G, Henry RM, et al. Local stiffness of the carotid and femoral artery is associated with incident cardiovascular events and all-cause mortality: the Hoorn study. J Am Coll Cardiol. 2014;63(17):1739-47.

19. Bonapace S, Rossi A, Cicoira M, Targher G, Valbusa F, Benetos A, Vassanelli C. Increased aortic pulse wave velocity as measured by echocardiography is strongly associated with poor prognosis in patients with heart failure. J Am Soc Echocardiogr. 2013 Jul;26(7):714-20. doi: 10.1016/j.echo.2013.03.022.

20. Yaman M, Arslan U, Bayramoğlu A, Bektaş O, Karataş A. Color M-mode echocardiography-derived propagation velocity of descending aorta decreases with aging. Ther Clin Risk Manag. 2017 May 24;13:669-674. doi: 10.2147/TCRM.S133011.